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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/624,645	07/23/2003	Claudio Pisano	2818-167	6903

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 05/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/624,645	PISANO ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment dated 3-15-06 is acknowledged.

Claims included in the prosecution are 43-70.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

2. Claims 29-33, 38-40 and 42 are rejected under 35 U.S.C. 102(a) as being anticipated by Wang et al (J. Med. Chem. 1998) of record.

Wang et al disclose cationic liposome compositions containing claimed alky acyl carnitine esters for gene delivery. The fatty acid groups are oleyl or myristoyl, palmitoyl or stearoyl groups. The liposomes contain helper lipid, cholesterol. The liposomes are administered intravenously (abstract, Scheme 1 on page 2208, Tables 3 and 4 on page 2211, page 2214, col. 2).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 43-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al by itself or in combination with Burke (5,552,156) by itself or in further combination with Stracher (5,008,288).

The teachings of Wang et al have been discussed above. What is lacking in Wang et al is the teaching of the use of claimed drugs such as anti-cancer drugs, camptothecins in particular.

Burke teaches that liposome stabilize camptothecin derivatives (abstract, examples and claims).

Stracher teaches that because of the presence of carnitine or its derivatives as part of liposomal structure, the drug containing liposomes will be delivered in much greater amounts to the desired target organs and much less is metabolized by the liver (abstract, col. 17, line 51 through col. 18, line 44).

It would have been obvious to one of ordinary skill in the art to use the liposomes of Wang et al to delver drugs other than genes, such as anti-cancer drugs or cosmetic agents with a reasonable expectation of success since liposomes are known drug and cosmetic agent carriers. One of ordinary skill in the art would use camptothecin derivatives as drugs since they are known to be encapsulated in liposomes because of stabilization by liposomes as taught by Burke. One of ordinary skill in the art would be motivated to use carnitine derivatives containing liposomes of Wang et al for the delivery of camptothecin derivatives of Burk since Stracher teaches the advantages of the presence of carnitine derivatives in liposomal structure in the drug delivery.

In view of applicant's arguments on page 10 that Wang (J. Med. Chem., 1998) alone should not be considered applicable, the rejection of claims over Wang alone has been withdrawn. Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that it is well known by those skilled in the art that not all liposomes are able to complex DNA and/or to crown drugs and In fact, the capacity of a liposome to complex DNA and/or to crown a drug is not predictable a priori. These arguments are not persuasive; instant claims recite generic 'pharmaceutically active compounds' and 'genes' come under the category of 'drugs'. The examiner cites US 6,008202 in this context (see col. 7, line 61 through col. 8, line 17). Furthermore, liposomes are known carriers for a variety of drugs and macromolecules and therefore, one of ordinary skill in the art would be able to encapsulate any active agent based on the teachings of Wang with a reasonable expectation of success. The examiner cites US 6,171,614 in this context (see col. 14, line 39 through col. 16, line 35). Applicant has not shown any unexpected results using the liposomes taught by Wang for other pharmaceutically active compounds. In addition, if one were to follow applicant's arguments of unpredictability, then would expect the same unpredictability in encapsulating numerous compounds, which come under the term, 'pharmaceutically active compounds' and 'substance with cosmetic activity'.

Applicant argues that Burke (5,552,156) relates to liposomes of dimyristoyl phosphatidylcholine derivatives and camptothecin derivatives such as Topotecan and that the present invention relates to liposomes of carnitine derivatives, and camptothecin derivatives such as gimatecan. Applicant further argues that those skilled

in the art also knows that not all liposomes are able to crown camptothecin and that the art knows that the capacity of a liposome to crown a drug depends upon its shape and size. These arguments are not persuasive. First of all, applicant has not presented any evidence to this effect and has not shown any unexpected results. Secondly, the claims are not drawn just to a specific camptothecin and liposomes containing only claimed carnitine derivatives. According to dependent claims, the liposomes contain other phospholipids or cholesterol besides carnitine derivatives. Burke teaches several other phospholipids besides dimyristoylphosphatidylcholine which could be used to form liposomes and encapsulate camptothecin derivatives (col. 6, lines 16-34) and based on his teachings one of ordinary skill in the art would reasonably predict the ability of the liposomes to encapsulate any drug including camptothecin derivatives. Furthermore, the reference of Wang teaches the claimed phospholipid, dioleoylphosphatidylcholine.

Applicant argues that the carnitine derivatives mentioned by Stracher are completely different from the carnitine derivatives claimed in the present invention; the examiner recognizes that, but points out that the Stracher shows the knowledge in the art of the preparation of liposomes using either carnitine or carnitine derivatives for the drug delivery. One of ordinary skill in the art therefore, would reasonably expect similar liposome formation with other carnitine derivatives.

5. Claims 43-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hsu (5,653,996) in combination with Wang et al cited above.

Hsu discloses liposomal compositions for the delivery of therapeutic or cosmetic agents. The agents include plasmids (DNA), a variety of passenger molecules (col. 4, lines 53-55, col. 6, line 10 through col. 7, line 42, col. 15, lines 1-9).

What is lacking in Hsu is the teaching of the inclusion of claimed carnitine derivatives.

Wang as discussed above teaches the ability of the claimed carnitine derivatives to form liposomes by themselves or in combination with other bilayer forming phospholipids (abstract).

It would have been obvious to one of ordinary skill in the art to use the liposomes of Wang in the teachings of Hsu for the delivery of therapeutic as well as cosmetic agents with a reasonable expectation of success since both Wang and Hsu are directed to liposomes and liposomes are carriers of active agents.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/G S Kishore/

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK